1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Primopen 300 mg/ml suspension for injection for cattle, pigs and horses.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Active substance:

Each ml contains:

Benzylpenicillin (procaine) monohydrate	300 mg
equivalent to benzylpenicillin	170 mg

Excipients:

Qualitative composition of excipients and other constituents	**Quantitative composition if that information is essential for proper administration of the veterinary medicinal product**
Sodium citrate	
Povidone K30	
Disodium edetate	0.55 mg
Sodium methyl parahydroxybenzoate (E219)	1.15 mg
Sodium formaldehyde sulfoxylate	2.50 mg
Hydrochloric acid dilute (for pH adjustment)	
Lecithin	
Water for injections	

White to almost white, homogeneous suspension.

3. CLINICAL INFORMATION

3.1 Target species

Cattle, pigs and horses.

3.2 Indications for use for each target species

For the treatment of infections caused by penicillin-sensitive bacteria.

3.3 Contraindications

Do not use in rabbits, guinea pigs, hamsters or gerbils.
Do not use intravenously.
Do not use in cases of hypersensitivity to the active substances, cephalosporins, procaine or to any of the excipients.

3.4 Special warnings

The product will not be effective against beta lactamase producing organisms.

After absorption, benzylpenicillin poorly penetrates biological membranes (e.g., blood-brain barrier) since it is ionised and poorly lipid soluble. Use of the product for treatment of meningitis or CNS infections due to e.g., *Streptococcus suis* or *Listeria monocytogenes* may not be efficacious. Furthermore, benzylpenicillin penetrates mammalian cells poorly and hence this product may have little effect in treating intracellular pathogens e.g., *Listeria monocytogenes*.

Elevated MIC values or bi-modal distribution profiles suggesting acquired resistance have been reported for the following bacteria:
- *Glaesserella parasuis, Staphylococcus* spp. causing MMA/PPDS, *Streptococcus* spp. and *S. suis* in pigs;
- *Fusobacterium necrophorum* causing metritis and *Mannheimia haemolytica* (only in some member states), as well as *Bacteroides* spp., *Staphylococcus chromogenes, Actinobacillus lignieresii* and *Trueperella pyogenes* in cattle.

Use of the veterinary medicinal product may result in a lack of clinical efficacy when treating infections caused by these bacteria.

3.5 Special precautions for use

Special precautions for safe use in the target species:

Use of the product should be based on identification and susceptibility testing of the target pathogens. If this is not possible, therapy should be based on epidemiological information and knowledge of susceptibility of the target pathogens at farm level, or at local/regional level.

Use of the product should be in accordance with official, national and regional antimicrobial policies.
Use of the product deviating from the instructions given in the SPC may increase the prevalence of bacteria resistant to benzylpenicillin and may decrease the effectiveness of treatment with other penicillins and cephalosporins due to the potential for cross-resistance.

Special precautions to be taken by the person administering the veterinary medicinal product to animals:

Penicillins and cephalosporins may cause hypersensitivity (allergy) following injection, inhalation, ingestion or skin contact. Hypersensitivity to penicillin may lead to cross reactions to cephalosporins and vice versa. Allergic reactions to these substances are occasionally serious.
People with known hypersensitivity to penicillin should avoid contact with the veterinary medicinal product.
Handle this product with great care to avoid exposure, taking all recommended precautions.
If you develop symptoms following exposure, such as skin rash, you should seek medical advice and show the doctor this warning. Swelling of the face, lips or eyes, or difficulty breathing are more serious symptoms and require urgent medical attention.
In case of accidental contact with eyes, rinse immediately with copious amounts of water.
Accidental spillage on the skin should be washed immediately with soap and water.
In case of accidental self-injection, seek medical advice immediately and show the package leaflet or the label to the physician.

Special precautions for the protection of the environment:

Not applicable.

3.6 Adverse events

Cattle:

Very rare (<1 animal / 10,000 animals treated, including isolated reports):	Allergic reaction

Horses:

Very rare (<1 animal / 10,000 animals treated, including isolated reports):	Allergic reaction Death
Undetermined frequency (cannot be estimated from the available data):	Locomotor disturbance Behavioural disorder

Pigs:

Very rare (<1 animal / 10,000 animals treated, including isolated reports):	Allergic reaction
Undetermined frequency (cannot be estimated from the available data):	Vaginal discharge[1] Pyrexia[2], Listless[2] Vomiting[2] Incoordination[2], Shivering[2]

[1]: In pregnant sows and gilts could be associated with abortion.
[2]: Transient.

Systemic toxic effects have been observed in young piglets, which are transient but can be potentially lethal, especially at higher doses.

Reporting adverse events is important. It allows continuous safety monitoring of a veterinary medicinal product. Reports should be sent, preferably via a veterinarian, to either the marketing authorisation holder or its local representative or the national competent authority via the national reporting system. See the package leaflet for respective contact details.

3.7 Use during pregnancy, lactation or lay

Pregnancy and lactation:

Laboratory studies in animals have not produced any evidence of teratogenic, fetotoxic or maternal toxic effects.
The safety of this veterinary medicinal product has not been established during pregnancy and lactation.

Use only according to the benefit-risk assessment by the responsible veterinarian.
See also section 3.6.

3.8 Interaction with other medicinal products and other forms of interaction

Benzylpenicillin is bactericidal. Avoid concurrent use of bactericidal and bacteriostatic antibiotics.
There is cross-resistance between penicillins and other beta-lactam antibiotics.

3.9 Administration routes and dosage

For intramuscular use.

Administer by deep intramuscular injection once daily. The treatment duration is 3 to 7 days.
The appropriate treatment duration should be chosen based on the clinical needs and individual recovery of the treated animal. Consideration should be given to the accessibility of the target tissue and characteristics of the target pathogen.
The recommended daily dose is 12 mg of benzylpenicillin procaine/kg body weight equivalent to 1 ml/25 kg body weight/day.
The maximum volume to be administered per injection site is 15.5 ml in cattle and 3.2 ml in pigs.
To ensure a correct dosage, body weight should be determined as accurately as possible.

Clean the area of the injection site and swab with spirit.
Do not use the same injection site more than once during a course of treatment.

Shake well before use.
The bottle may be broached up to 20 times.

3.10 Symptoms of overdose (and where applicable, emergency procedures and antidotes)

Penicillin is a compound with a very high therapeutic index.
However, overdosing in young animals and horses should be avoided in order to prevent procaine poisoning.

3.11 Special restrictions for use and special conditions for use, including restrictions on the use of antimicrobial and antiparasitic veterinary medicinal products in order to limit the risk of development of resistance

Not applicable.

3.12 Withdrawal periods

Cattle
Meat and offal: 6 days for treatment duration 3-5 days.
8 days for treatment duration 6-7 days.

Milk: 4 days (96 hours).

Pigs
Meat and offal: 4 days for treatment duration 3-5 days.
6 days for treatment duration 6-7 days.

Horses
Meat and offal: 180 days for treatment duration 3-5 days.
182 days for treatment duration 6-7 days.

Not authorised for use in horses producing milk for human consumption.

4. PHARMACOLOGICAL INFORMATION

4.1 ATCvet code:

QJ01CE09

4.2 Pharmacodynamics

Penicillin is a beta-lactam antibiotic which has bactericidal activity against mainly Gram-positive bacteria and some Gram-negative aerobes such as:

- Gram-positive bacteria: *Trueperella pyogenes, Erysipelothrix rhusiopathiae, Listeria* spp., *Staphylococcus* spp. (non-penicillinase producing) and *Streptococcus spp*. susceptible to penicillin, except for *Staphylococcus Intermedius and pseudointermedius*.
- Gram-negative bacteria: *Pasteurella multocida* and *Mannheimia haemolytica* susceptible to penicillin.

Benzylpenicillin exerts its effect on multiplying bacteria blocking the biosynthesis of the bacterial wall. The resistance of bacteria is due to beta-lactamase (penicillinase) inactivation, alteration or inaccessibility of the drug target.

Clinical breakpoints for penicillins based on European Committee of Antimicrobial Susceptibility Testing, version 9.0, 2019 and VetPath4 (2019):

Bacterial groups	**MIC breakpoint (µg/ml)**	
	Susceptible	**Resistant**
Listeria monocytogenes.	S≤1	R>1
Pasteurella multocida	S≤0.5	R>0.5
Staphylococcus spp.	S≤0.125	R>0.125
Streptococcus spp.	S≤0.25	R>0.25
Mannheimia haemolytica	S≤0.5	R>0.5

In the case of *Trueperella pyogenes, Erysipelothrix rhusiopathiae* no breakpoints have been determined.

The following Minimum Inhibitory Concentrations (MIC) have been determined by VetPath4 programme (2019) for penicillin in target bacteria isolated from diseased animals throughout Europe:

Organisms	**MIC_{50} (µg/ml)**	**MIC_{90}(µg/ml)**
Mannheimia haemolytica	0.12	0.5
Pasteurella multocida	0.12	0.25
Staphylococcus aureus	0.06	4
Streptococcus suis	0.03	0.5
Trueperella pyogenes	0.008	0.015

Enterobacterales, *Bacteroides fragilis*, most *Campylobacter* spp., *Nocardia* spp. and *Pseudomonas* spp. as well as beta-lactamase–producing *Staphylococcus* spp. are resistant.

4.3 Pharmacokinetics

The following pharmacokinetic data were recorded in the target species following the single administration of the recommended dose:

Species	**C_{max} (µg/ml)**	**T_{max} (hours)**
Cattle	1.14	2.03
Pigs	2.07	1.25
Horses	0.93	4.20

Penicillin is widely distributed in the extracellular fluids after absorption and eliminated almost entirely by the kidneys.

5. PHARMACEUTICAL PARTICULARS

5.1 Major incompatibilities

In the absence of compatibility studies, this veterinary medicinal product must not be mixed with other veterinary medicinal products.

5.2 Shelf life

Shelf-life of the veterinary medicinal product as packaged for sale: 3 years.
Shelf-life after first opening the immediate packaging: 28 days.

5.3 Special precautions for storage

Store in a refrigerator (2°C - 8°C).
Do not freeze.
Keep the bottle in the outer carton in order to protect from light.

5.4 Nature and composition of immediate packaging

Type II colourless glass bottles and colourless polyethylene terephthalate (PET) bottles, closed with chlorobutyl rubber stopper (Type I) and flip-off aluminium collar with tamper-evident polypropylene seal, in a cardboard box.

Pack-sizes:
Cardboard box with 1 glass or PET bottle of 100 ml
Cardboard box with 1 glass or PET bottle of 250 ml
Cardboard box with 10 PET bottles of 100 ml
Cardboard box with 30 PET bottles of 100 ml
Cardboard box with 6 PET bottles of 250 ml

Not all pack sizes may be marketed.

5.5 Special precautions for the disposal of unused veterinary medicinal products or waste materials derived from the use of such products

Medicines should not be disposed of via wastewater or household waste.

Use take-back schemes for the disposal of any unused veterinary medicinal product or waste materials derived thereof in accordance with local requirements and with any national collection systems applicable to the veterinary medicinal product concerned.

6. NAME OF THE MARKETING AUTHORISATION HOLDER

FATRO S.p.A

7. MARKETING AUTHORISATION NUMBER(S)

VPA10836/007/001

8. DATE OF FIRST AUTHORISATION

18/09/2020

9. DATE OF THE LAST REVISION OF THE SUMMARY OF THE PRODUCT CHARACTERISTICS

16/08/2024

10. CLASSIFICATION OF VETERINARY MEDICINAL PRODUCTS

Veterinary medicinal product subject to prescription.

Detailed information on this veterinary medicinal product is available in the Union Product Database (https://medicines.health.europa.eu/veterinary).